DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

ROCHE DIAGNOSTICS OPERATIONS (RDO)
NOEL MENCIAS
REGULATORY AFFAIRS CONSULTANT
9115 HAGUE ROAD
INDIANAPOLIS IN 46250

January 28, 2015

Re: K143691

Trade/Device Name: LDLC3 LDL-Cholesterol Gen.3
Regulation Number: 21 CFR 862.1475
Regulation Name: Lipoprotein test system
Regulatory Class: I, Meets limitations of the exemption as per 21 CFR 862.9 (c)(4)
Product Code: LBR
Dated: December 23, 2014
Received: December 24, 2014

Dear Noel Mencias:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Katherine Serrano -S

For: Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES Food and Drug Administration **Indications for Use**	Form Approved: OMB No. 0910-0120 Expiration Date: January 31, 2017 *See PRA Statement below.*

510(k) Number *(if known)*
k143691

Device Name
LDLC3 LDL-Cholesterol Gen.3

Indications for Use *(Describe)*

The LDL-Cholesterol Gen. 3 assay is an in-vitro test for the quantitative determination of LDL-cholesterol in human serum and plasma on Roche/Hitachi cobas c systems. Lipoprotein measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

510(k) Summary for LDLC3 LDL-Cholesterol Gen. 3

Date prepared:	December 23, 2014
Purpose of submission	In accordance with 21 CFR 807.87, Roche Diagnostics hereby submits official notification as required by Section 510(k) of the Federal Food, Drug and Cosmetics Act of our intention to market the device described in this Premarket Notification [510(k)]. This candidate device is a new reagent that was developed by Roche Diagnostics. The previous generation of reagent, LDL-Cholesterol plus 2nd generation, was cleared in 510(k) k974733 and serves as the predicate device. The candidate and predicate devices use the same calibrator and controls. Only the reagents differ. This submission presents data to support clearance of this new reagent.
Measurand	Lipoprotein
Type of test	Quantitative homogeneous enzyme colorimetric method
Applicant	Noel B. Mencias, Regulatory Affairs Consultant Roche Diagnostics 9115 South Hague Road Indianapolis, IN 46250 Telephone: (317) 521-3172 Fax: (317) 521-2324 Email: noel.mencias@roche.com
Candidate device names	Proprietary name: LDLC3 LDL-Cholesterol Gen. 3 Common name: LDL-Cholesterol Gen. 3 Classification name: Lipoprotein Test System (21 CFR 862.1475)

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510(k) Summary for LDLC3 LDL-Cholesterol Gen. 3, Continued

Regulatory information

Product Code	Classification	Regulation	Panel
LBR	Class I	21 CFR 862.1475 (Lipoprotein test system)	Clinical Chemistry 75

LDLC3 LDL-Cholesterol Gen. 3 meets the limitation of exemption per 21 CFR 862.9 (c)(4) - for cardiovascular risk.

Intended use

The **LDL-Cholesterol Gen. 3** assay is intended for use as an in vitro test for the quantitative determination of LDL-Cholesterol in human serum and plasma on Roche/Hitachi **cobas c** systems.

Indications for use

The LDL-Cholesterol Gen. 3 assay is an in-vitro test for the quantitative determination of LDL-cholesterol in human serum and plasma on Roche/Hitachi **cobas c** systems. Lipoprotein measurements are used in the diagnosis and treatment of lipid disorders (such as diabetes mellitus), atherosclerosis, and various liver and renal diseases.

Special conditions for use

For prescription use only.

Special instrument requirements

For use on the Roche/Hitachi **cobas c** clinical chemistry analyzer.

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510(k) Summary for LDLC3 LDL-Cholesterol Gen. 3, Continued

Candidate device description

The LDL-Cholesterol Gen. 3 assay is a homogeneous enzyme colorimetric assay which provides the quantitative measurement of LDL-cholesterol in human serum and plasma.

Reagents are packaged in a cassette labeled with their instrument positioning R1 (Reagent 1) and R2 (Reagent 2).

- R1 contains Bis-trisb) buffer: 20.1 mmol/L, pH 7.0; 4-aminoantipyrine:0.98 mmol/L; ascorbic oxidase (AOD, Acremonium spec.): ≥ 66.7 µkat/L; peroxidase (recombinant from Basidiomycetes): ≥ 166.7 µkat/L; BSA: 4.0 g/L; preservative
- R2 contains MOPSc) buffer: 20.1 mmol/L, pH 7.0; EMSE: 2.16 mmol/L, cholesterol esterase (Pseudomonas spec.): ≥ 33.3 µkat/L; cholesterol oxidase (recombinant from E.coli)): ≥ 31.7 µkat/L; peroxidase (recombinant from Basidiomycetes): ≥ 333.3 µkat/L; BSA: 4.0 g/L; detergents; preservative

Predicate device

Roche Diagnostics claims substantial equivalence to LDL-Cholesterol plus 2^{nd} generation reagent on the **cobas c** 501. The reagent was originally cleared in k974733 on the Boehringer Mannheim/Hitachi clinical chemistry analyzers, and later cleared in a Special 510(k) k012287 on COBAS INTEGRA. The application to the **cobas c** 501 analyzer was cleared on October 3, 2006 in k060373/A001 following the FDA Policy Document "Replacement Reagent and Instrument Family Policy – 12/11/2003."

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510(k) Summary for LDLC3 LDL-Cholesterol Gen. 3, Continued

Substantial Equivalence – Assay Similarities

The following table compares the similar features of the candidate device to the predicate device that was cleared in 510(k) k974733.

Assay Comparison Similarities		
Feature	**Predicate Device: LDL_C Cholesterol Plus 2nd generation**	**Candidate Device: LDLC3 LDL-Cholesterol Gen. 3**
Intended Use	In vitro test for the quantitative determination of LDL-Cholesterol in human serum and plasma on Roche/Hitachi **cobas c** systems.	Same
Sample Types	Human Serum and Plasma	Same
Test Principle	Homogenous enzymatic colorimetric assay	Same
Reagent Shelf Life Stability	2-8 °C until expiration date	Same
Reagent On-Board Stability	12 weeks	Same
Measuring Range	0.10 – 14.2 mmol/L (3.86 - 548 mg/dL)	3.87 -549 mg/dL
Lower Limit of Measurement	LDL(lower detection limit) = 0.10 mmol/L (3.866 mg/dL)	LoB = 0.406 mg/dL LoD = 0.99 mg/dL LoQ = 2.28 mg/dL
Expected Values	Adult levels: Optimal: < 2.59 mmol/L (< 100 mg/dL) Near optimal/above optimal: 2.59-3.34 mmol/L (100-129 mg/dL) Borderline high: 3.37-4.12 mmol/L (130-159 mg/dL) High 4.14-4.89 mmol/L (160-189 mg/dL) Very high: ≥ 4.92 mmol/L (≥ 190 mg/dL)	Same
Traceability	This method has been standardized against the beta quantification method as defined in the recommendations in the LDL Cholesterol Method Certification Protocol for Manufacturers	Same

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510(k) Summary for LDLC3 LDL-Cholesterol Gen. 3, Continued

Substantial Equivalence – Assay Similarities (continued)

Assay Comparison Similarities		
Calibrator	Calibrator for automated systems (C.f.a.s) Lipids and deionized water as the zero calibrator. (C.f.a.s. cleared for use with LDL-Cholesterol in k011658	Same
Calibration frequency	Recalibrate after reagent lot change and as required following quality control procedures	Same
Controls	Precinorm L Precipath HDL/LDL-C PreciControl ClinChem Multi 1 PreciControl ClinChem Multi 2 PreciControl ClinChem Multi 1 and PreciControl ClinChem Multi 2 were cleared for use with LDL_C in 510(k) k102016	Same

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510(k) Summary for LDLC3 LDL-Cholesterol Gen. 3, Continued

Substantial Equivalence – Assay Difference

The following table compares the differences of the candidate device to the predicate device that was cleared in 510(k) k974733

Assay Comparison Differences		
Feature	**Predicate Device: LDL_C Cholesterol Plus 2nd generation**	**Candidate Device: LDLC3 LDL-Cholesterol Gen. 3**
Test Principle	In the presence of peroxidase, the hydrogen peroxide generated reacts with 4-aminoantipyrine and HSDA to form a purple-blue dye. The color intensity of this dye is directly proportional to the cholesterol concentration and is measured photometrically.	In the presence of peroxidase, the hydrogen peroxide generated reacts with 4-aminoantipyrine and EMSE to form a red purple dye. The color intensity of this dye is directly proportional to the cholesterol concentration and is measured photometrically.
Reagent Composition	**R1** MOPS (3-morpholinopropane sulfonic acid) buffer: 20.1 mmol/L, pH 6.5; HSDA: 0.96 mmol/L; ascorbate oxidase (Eupenicillium spec., recombinant): ≥50 µkat/L; peroxidase (horseradish): ≥167 µkat/L; preservative **R2** MOPS (3-morpholinopropane sulfonic acid) buffer: 20.1 mmol/L, pH 6.8; $MgSO4·7H2O$: 8.11 mmol/L; 4-aminoantipyrine: 2.46 mmol/L; cholesterol esterase (Pseudomonas spec.): ≥50 µkat/L; cholesterol oxidase (Brevibacterium spec., recombinant): ≥33.3 µkat/L; peroxidase (horseradish): ≥334 µkat/L; detergent; preservative	**R1** Bis-tris buffer: 20.1 mmol/L, pH 7.0; 4-aminoantipyrine: 0.98 mmol/L; ascorbic oxidase (AOD, Acremonium spec.): ≥ 66.7 µkat/L; peroxidase (recombinant from Basidiomycetes): ≥ 166.7 µkat/L; BSA: 4.0 g/L; preservative **R2** MOPS buffer: 20.1 mmol/L, pH 7.0; EMSE: 2.16 mmol/L, cholesterol esterase (Pseudomonas spec.): ≥ 33.3 µkat/L; cholesterol oxidase (recombinant from E.coli)): ≥ 31.7 µkat/L; peroxidase (recombinant from Basidiomycetes): ≥ 333.3 µkat/L; BSA: 4.0 g/L; detergents; preservative

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510(k) Summary for LDLC3 LDL-Cholesterol Gen. 3, Continued

Summary of tests

The following performance data were provided in support of the substantial equivalence determination:

Limit of Blank according to CLSI EP17-A2
Limit of Detection according to CLSI EP17-A2
Limit of Quantitation according to CLSI EP17-A2
Precision according to CLSI EP5-A2
Linearity according to CLSI EP6-A
Rerun Function Check (Post Dilution Factor)
Recovery in Controls
Method Comparison
Verification of plasma as sample material
Drug Interferences
Endogenous Interferences in serum/plasma
Stability & Calibration frequency

All performance specifications were met.

Test Principle

Cholesterol esters and free cholesterol in LDL are measured on the basis of a cholesterol enzymatic method using cholesterol esterase and cholesterol oxidase in the presence of surfactants which selectively solubilizes only LDL. The enzyme reactions to the lipoproteins other than LDL are inhibited by surfactants and a sugar compound. Cholesterol in HDL, VLDL and chylomicron is not determined.

Cholesterol esters are broken down quantitatively into free cholesterol and fatty acids by cholesterol esterase.

In the presence of oxygen, cholesterol is oxidized by cholesterol oxidase to Δ4-cholestenone and hydrogen peroxide.

In the presence of peroxidase, the hydrogen peroxide generated reacts with 4-aminoantipyrine and EMSE* to form a red purple dye. The color intensity of this dye is directly proportional to the cholesterol concentration and is measured photometrically.

*N-ethyl-N-(3-methylphenyl)-N-succinylethylenediamine

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510(k) Summary for LDLC3 LDL-Cholesterol Gen. 3, Continued

Detection Limit

LoB, LoD, and LoQ studies were performed based upon CLSI EP17-A2.

LoB Protocol: One analyte free sample was tested in five-fold determinations on two analyzers over three days, for a total of N=60 determinations. Three lots of reagent were used for testing. The LoB is determined as the 95th percentile of the 60 measured values.

LoD Protocol: Five low-analyte samples were measured in singlicate on two analyzers over three days. Three lots of reagent were used for testing.

LoD was calculated as:

$$\text{LoD} = \text{LoB} + 1.653 \times SD_{tot}$$

Where:

$$SD_{total} = \text{Square root } [0.2 \times ((SD_{sample\ 1})^2 + (SD_{sample 2})^2 + (SD_{sample\ 3})^2 + (SD_{sample 4})^2 + (SD_{sample\ 5})^2\ )].$$

LoQ Protocol: A low-level sample set of five samples were tested in five replicates per sample on five days with three reagent lots, one run per day on one analyzer. The mean, the SD, and the %CV of 5 days were calculated for each sample. The mean concentration was plotted versus the %CV and LoQ is determined based on the precision at 10% CV.

The LoB, LoD, and LoQ claims represent the specifications for each.

	Result (mg/dL)	Claim (mg/dL)
Limit of Blank	0.406	3.87
Limit of Detection	0.99	3.87
Limit of Quantitation	2.28	3.87

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510(k) Summary for LDLC3 LDL-Cholesterol Gen. 3, Continued, Continued

Precision

Precision was determined according to CLSI EP5-A2 with one analyzer and 3 reagent lots using 5 human serum sample pools and two control samples (4 aliquots per run, 1 run per day, 21 days). The following results were obtained:

Repeatability Summary

Specimen	Mean mg/dL (mmol/L)	SD mg/dL (mmol/L)	CV (%)
Precinorm L	104 (2.69)	0.8 (0.02)	0.7
Precipath HDL/LDL-C	191 (4.93)	1.2 (0.03)	0.7
Human Serum 1	11.7 (0.302)	0.2 (0.004)	1.2
Human Serum 2	113 (2.93)	0.8 (0.02)	0.7
Human Serum 3	303 (7.83)	2.3 (0.06)	0.7
Human Serum 4	142 (3.67)	1.2 (0.03)	0.7
Human Serum 5	526 (13.6)	4.3 (0.11)	0.8

Intermediate Precision

Specimen	Mean mg/dL (mmol/L)	SD mg/dL (mmol/L)	CV (%)
Precinorm L	104 (2.69)	2.3 (0.06)	2.3
Precipath HDL/LDL-C	194 (5.02)	4.2 (0.11)	2.1
Human Serum 1	12.2 (0.316)	0.3 (0.008)	2.5
Human Serum 2	117 (3.03)	2.3 (0.06)	2.1
Human Serum 3	315 (8.14)	6.2 (0.16)	1.9
Human Serum 4	143 (3.71)	3.1 (0.08)	2.1
Human Serum 5	530 (13.7)	10.8 (0.28)	2.0

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510(k) Summary for LDLC3 LDL-Cholesterol Gen. 3, Continued, Continued

Analytical Specificity – interference from common drugs, Simvastatin, Bezafibrate, and Nicotinic Acid

Sixteen commonly used drugs were examined for potential interference on measurement with LDL-Cholesterol Gen.

Two sample pools, containing a low (approximately 100 mg/dL) and high (approximately 400 mg/dL) concentration of LDL are used. These sample pools are divided into an appropriate number of aliquots. One aliquot is not spiked with the drugs and it is used as the reference sample for LDL concentration. The LDL concentration in the sample is determined with n = 3 measurements on a **cobas c** 501 analyzer.

The other sample aliquots, with either the high or low LDL concentrations, are spiked with the respective amount of drug. The LDL concentration of the spiked aliquots are determined in triplicate and the mean of the triplicate determinations is compared to the LDL concentration determined for the reference aliquot (mean of n=3).

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510(k) Summary for LDLC3 LDL-Cholesterol Gen. 3, Continued, Continued

Analytical Specificity – interference from common drugs, Simvastatin, Bezafibrate, and Nicotinic Acid, Simvastatin, Bezafibrate, and Nicotinic Acid (continued)

The table below summarizes the common drug interferences data:

Drug	Highest Concentration Shown Not to Interfere with LDLC3 (drug concentrations in mg/L)
Acetylcysteine	553
Ampicillin-Na	1000
Ascorbic acid	5000
Cyclosporine	5
Cefoxitin	2500
Heparin	5000 U
Levodopa	20
Methyldopa +1.5	20
Metronidazole	200
Phenylbutazone	400
Doxycyclin	50
Acetylsalicylic Acid	1000
Rifampicin	60
Acetaminophen	200
Ibuprofen	500
Theophylline	100

Additional testing was done on Simvastatin, Bezafibrate, and Nicotinic Acid. The table below summarizes the interference data:

Drug	Highest Concentration Shown Not to Interfere with LDLC3 (drug concentrations in mg/L)
Simvastatin	16
Bezafibrate	120
Nicotinic Acid	400

All data passed the following acceptance criteria:
Difference in recovery to the reference sample: ≤ ± 10%

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510(k) Summary for LDLC3 LDL-Cholesterol Gen. 3, Continued, Continued

Analytical Specificity – interference from VLDL, HDL, Chylomicrons

The effects of interference by VLDL-cholesterol, HDL-cholesterol, Chylomicrons on the LDLC3 test system was tested.

HDL-cholesterol: Two sample pools, containing a low and high concentration of LDL were used. These sample pools were divided into two aliquots. One aliquot was not spiked with HDL and it was used as the reference sample for LDL concentration. The LDL concentration in the sample was determined with n = 3 measurements on a **cobas c** 501 analyzer.

The other sample aliquot, with either the high or low LDL concentrations, was spiked with the respective amount of HDL. The LDL concentration of the spiked aliquots were determined in triplicate and the mean of the triplicate determinations was compared to the LDL concentration determined for the reference aliquot (mean of n=3).

The mean of the triplicate determinations was compared to the LDL concentration determined for the reference aliquot (mean of n=3).

VLDL-cholesterol: VLDL were isolated from fresh human serum by ultracentrifugation method. Two sample pools, containing a low and high concentration of LDL were used. The samples were spiked with increasing amounts of VLDL fraction with increasing amounts of VLDL concentrations.

The sample pools were split into two aliquots. One aliquot was spiked with VLDL-fraction the second was diluted with 0.9% NaCl as the reference.

The mean of the duplicate determinations is compared to the LDL concentration determined for the reference aliquot (mean of n=2).

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510(k) Summary for LDLC3 LDL-Cholesterol Gen. 3, Continued, Continued

Analytical Specificity – interference from VLDL, HDL, Chylomicrons (continued)

Chylomicrons (Triglycerides): Chylomicrons were separated from fresh non-fasting human samples by centrifugation. Four sample pools**, containing a low and high concentration of LDL were used. The samples were spiked with increasing amounts of chylomicrons. Triglycerides concentrations were measured in all samples. The sample pools were split into two aliquots. One aliquot was spiked with chylomicrons the second was diluted with 0.9% NaCl. The mean of the duplicate determinations was compared to the LDL concentration determined for the reference aliquot (mean of n=2). ** The four samples contain chylomicron concentrations ≥ 2000 mg/dL Triglycerides. Additional samples with lower concentrations of Chylomicron Triglycerides < 2000 Triglycerides were tested.

All data passed the following acceptance criteria:

≤± 10% in recovery
VLDL-Cholesterol: ≤ 140 mg/dL
HDL- Cholesterol: ≤ 75 mg/dL
Chylomicrons: ≤ 2000 mg/dL triglycerides

Analytical Specificity – interference from endogenous substances

The reagent was evaluated with three endogenous substances, hemoglobin, Lipemia (Intralipid), and Bilirubin for potential interference with the measurement of LDLC3.

One pool of human serum was spiked with the interferent. A second pool of human serum contained none. The two pools were mixed in different ratios to yield a dilution series with varying concentrations of the interferent.

The resulting sample series (10 dilution steps per sample) were tested in triplicate and the mean values used to calculate % recovery, by comparing the measured concentration to the expected concentration (which is the LDL concentration when no interferent was added).

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510(k) Summary for LDLC3 LDL-Cholesterol Gen. 3, Continued, Continued

Analytical Specificity – interference from endogenous substances (continued)

The endogenous interference data are summarized in the table. Interference was tested at two levels of reagent.

	no interference up to	Claim as it appears in the labeling.
Lipemia Level 1	1385 L index	No significant interference up to an L index of 1000 (approximate Intralipid concentration: 1000 mg/dL).
Lipemia Level 2	1967 L index	
Hemolysis Level 1	1392 H index	No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 1000 mg/dL).
Hemolysis Level 2	1463 H index	
Unconjugated Bilirubin Level 1	77 I index	No significant interference up to an I index of 60 (approximate conjugated and unconjugated bilirubin concentration: 60 mg/dL).
Unconjugated Bilirubin Level 2	65 I index	
Conjugated Bilirubin Level 1	71 I index	
Conjugated Bilirubin Level 2	68 I index	

<u>All data passed the following acceptance criteria</u>:

≤ ± 10%

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510(k) Summary for LDLC3 LDL-Cholesterol Gen. 3, Continued, Continued

Matrix Comparison

Lithium-heparin, K_2-EDTA and K_3-EDTA are permissible anticoagulants for use with this reagent because they do not interfere with recovery of LDL-Cholesterol Gen. 3. The effect of the presence of anticoagulants on analyte recovery was determined by method comparison, obtained from samples drawn into serum and different types of plasma collection tubes (K2 EDTA, K3 EDTA, Li Heparin, and Gel Separation). One reagent lot was tested with two runs, one replicate per sample with full tubes as follows:

	Range (mg/dL)	# Samples
Gel Separation	12.3 - 495	59
Li-heparin	12.3 - 495	59
K2-EDTA	12.3 - 495	57
K3-EDTA	12.3 - 495	59

Comparisons with plasma vs. serum were calculated with the following results for full tubes which passed specification :

Serum vs. Gel Separation P/B: $y = 1.004x + 0.091$, $r = 1.000$

Serum vs. Li-heparin P/B: $y = 0.99x – 1.50$, $r = 0.999$

Serum vs. K2-EDTA P/B: $y = 0.98x – 0.248$, $r = 1.000$

Serum vs. K3-EDTA P/B: $y = 0.95x - 0.246$, $r = 0.999$

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510(k) Summary for LDLC3 LDL-Cholesterol Gen. 3, Continued, Continued

Linearity

Linearity was assessed according to CLSI EP6-A with one batch of reagent, in one run, and with samples measured in triplicate. Two separate dilution series differing by sample type (serum and plasma) were prepared with 14 concentrations. Dilutions were made using 0.9% NaCl.

Evaluation is performed using a validated software tool provided by Roche Diagnostics Penzberg Biometry department. All the measured data of a dilution series are evaluated together in one regression analysis.

The software tool plots the measured values on the y-axis against the expected values on the x-axis and calculates regressions with first-order (y=a+bx, linear model), second-order (y=a+bx+cx2; quadratic model) and third-order polynomials (y=a+bx+cx2+dx3, cubic model). In the next step it examines which of the three polynomials best describes the course of the measured data. If the first-order polynomial gives the best fit, the tested measuring range is linear. If a better fit is obtained with a second- or third-order polynomial, the difference between this polynomial and the first-order polynomial is calculated.

In this case a third order polynomial is used. The linearity evaluation is not forced through the origin. Weighting is used: 1/conc quadratic.

Data passed the following acceptance criteria:
3.87 mg/dL-549 mg/dL: ≤ ± 10%

Measuring range supported by Linearity Data (mg/dL)

	Plasma	Serum
Range tested	3.66 - 584	3.53 - 565
Range found	3.66 - 584	3.53 - 565
Recommended measuring range	3.87 -549	3.87 -549

Linear Regression Equation for Serum:
$y = 1.0171x - 0.3682$ $r^2 = 0.9994$

Linear Regression Equation for Plasma:
$y = 1x + 0$ $r^2 = 0.9995$

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510(k) Summary for LDLC3 LDL-Cholesterol Gen. 3, Continued, Continued

Method Comparison to Predicate	A total of 100 human serum samples (including 5 spiked with human LDL rich serum and 2 diluted with 0.9% NaCl, range of 4.99 – 534 mg/dL) were tested in singlicate with the LDLC Gen2 assay and the LDLC3 reagent on **cobas c** 501. Sample size (n) = 100 Passing/Bablok y = 0.984x – 0.786 mg/dL r = 0.999
Conclusion	The submitted information in this premarket notification supports a substantial equivalence decision.